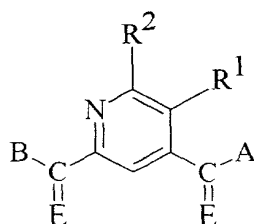


# CLAIMS

What is claimed is:

1. A method for inhibiting matrix metalloproteinase enzymes in a mammal comprising administering to the mammal an MMP inhibiting amount of a compound of Formula I



I

or a pharmaceutically acceptable salt thereof,

wherein:

R<sup>1</sup> and R<sup>2</sup> independently are hydrogen, halo, hydroxy, C<sub>1</sub>-C<sub>6</sub> alkyl,

C<sub>1</sub>-C<sub>6</sub> alkoxy, C<sub>2</sub>-C<sub>6</sub> alkenyl, C<sub>2</sub>-C<sub>6</sub> alkynyl, NO<sub>2</sub>, NR<sup>4</sup>R<sup>5</sup>, CN, or CF<sub>3</sub>;

E is independently O or S;

A and B independently are OR<sup>4</sup> or NR<sup>4</sup>R<sup>5</sup>;

R<sup>4</sup> and R<sup>5</sup> independently are H, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>2</sub>-C<sub>6</sub> alkenyl, C<sub>2</sub>-C<sub>6</sub>

alkynyl, (CH<sub>2</sub>)<sub>n</sub> aryl, (CH<sub>2</sub>)<sub>n</sub> cycloalkyl, (CH<sub>2</sub>)<sub>n</sub> heteroaryl, or R<sup>4</sup>

and R<sup>5</sup> when taken together with the nitrogen to which they are

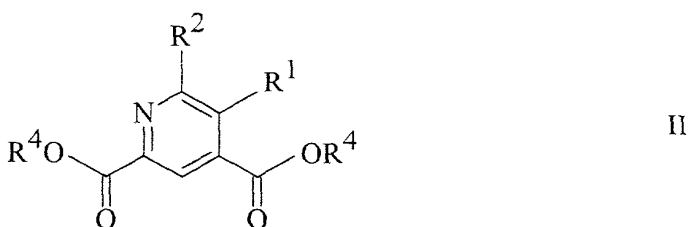
attached complete a 3- to 8-membered ring containing carbon

atoms and optionally containing a heteroatom selected from O, S,

or NH, and optionally substituted or unsubstituted,

n is an integer from 0 to 6.

2. A method for inhibiting matrix metalloproteinase enzymes in a mammal comprising administering to the mammal an MMP inhibiting amount of a compound of Formula II

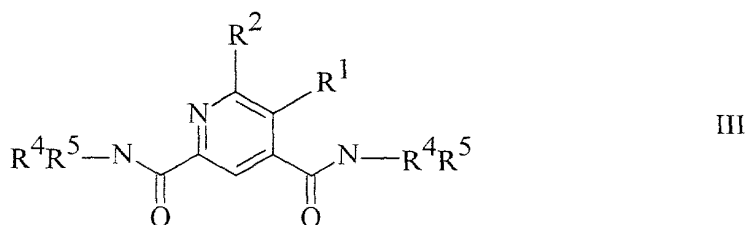


or a pharmaceutically acceptable salt thereof,

wherein R<sup>1</sup> and R<sup>2</sup> independently are hydrogen, halo, hydroxy, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-C<sub>6</sub> alkoxy, C<sub>2</sub>-C<sub>6</sub> alkenyl, C<sub>2</sub>-C<sub>6</sub> alkynyl, NO<sub>2</sub>, NR<sup>4</sup>R<sup>5</sup>, CN, or CF<sub>3</sub>; and

each R<sup>4</sup> and R<sup>5</sup> independently are H, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>2</sub>-C<sub>6</sub> alkenyl, C<sub>2</sub>-C<sub>6</sub> alkynyl, (CH<sub>2</sub>)<sub>n</sub> aryl, (CH<sub>2</sub>)<sub>n</sub> cycloalkyl, (CH<sub>2</sub>)<sub>n</sub> heteroaryl, or R<sup>4</sup> and R<sup>5</sup> when taken together with the nitrogen to which they are attached complete a 3- to 8-membered ring containing carbon atoms and optionally containing a heteroatom selected from O, S, or NH, and optionally substituted or unsubstituted, n is an integer of from 0 to 6

3. A method for inhibiting matrix metalloproteinase enzymes in a mammal comprising administering to the mammal an MMP inhibiting amount of a compound of Formula III

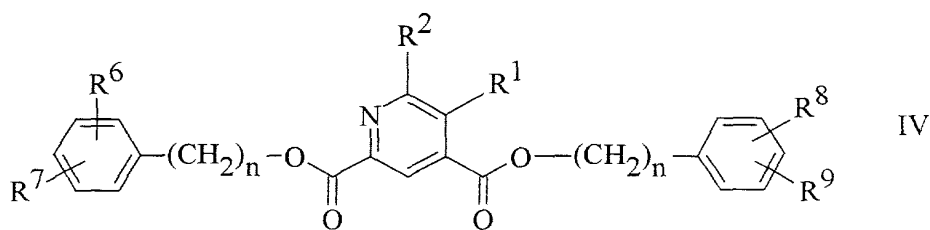


or a pharmaceutically acceptable salt thereof,

wherein R<sup>1</sup> and R<sup>2</sup> independently are hydrogen, halo, hydroxy, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-C<sub>6</sub> alkoxy, C<sub>2</sub>-C<sub>6</sub> alkenyl, C<sub>2</sub>-C<sub>6</sub> alkynyl, NO<sub>2</sub>, NR<sup>4</sup>R<sup>5</sup>, CN, or CF<sub>3</sub>;

$R^4$  and  $R^5$  independently are H,  $C_1$ - $C_6$  alkyl,  $C_2$ - $C_6$  alkenyl,  $C_2$ - $C_6$  alkynyl,  $(CH_2)_n$  aryl,  $(CH_2)_n$  cycloalkyl,  $(CH_2)_n$  heteroaryl, wherein each  $CH_2$  is optionally substituted by one or more  $C_1$ - $C_6$  alkyl, or  $R^4$  and  $R^5$  when taken together with the nitrogen to which they are attached complete a 3- to 8-membered ring containing carbon atoms and optionally containing a heteroatom selected from O, S, or NH, and optionally substituted or unsubstituted;  $n$  is an integer of from 0 to 6.

4. A method for inhibiting matrix metalloproteinase enzymes in a mammal comprising administering to the mammal an MMP inhibiting amount of a compound of Formula IV



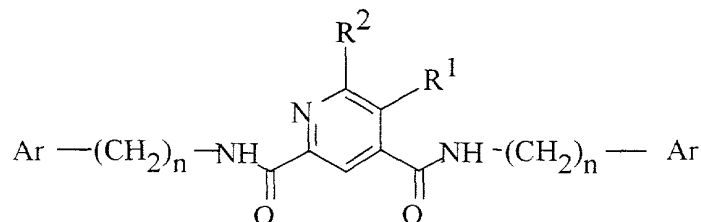
or a pharmaceutically acceptable salt thereof.  
wherein  $n$  is 0 to 6,

$R^1$  and  $R^2$  independently are hydrogen, halo, hydroxy,  $C_1$ - $C_6$  alkyl,  $C_1$ - $C_6$  alkoxy,  $C_2$ - $C_6$  alkenyl,  $C_2$ - $C_6$  alkynyl,  $NO_2$ ,  $NR^4R^5$ , CN, or  $CF_3$ ;

$R^4$  and  $R^5$  independently are H,  $C_1$ - $C_6$  alkyl,  $C_2$ - $C_6$  alkenyl,  $C_2$ - $C_6$  alkynyl,  $(CH_2)_n$  aryl,  $(CH_2)_n$  cycloalkyl,  $(CH_2)_n$  heteroaryl, wherein each  $CH_2$  is optionally substituted by one or more  $C_1$ - $C_6$  alkyl, or  $R^4$  and  $R^5$  when taken together with the nitrogen to which they are attached complete a 3- to 8-membered ring containing carbon atoms and optionally containing a heteroatom selected from O, S, or NH, and optionally substituted or unsubstituted, and

$R^6$ ,  $R^7$ ,  $R^8$ , and  $R^9$  independently are hydrogen, halo,  $C_1$ - $C_6$  alkyl,  $C_1$ - $C_6$  alkoxy, nitro, or  $NH_2$ .

5. A method for inhibiting matrix metalloproteinase enzymes in a mammal comprising administering to the mammal an MMP inhibiting amount of a compound of Formula V



V

or a pharmaceutically acceptable salt thereof,  
wherein n is 0 to 6;

$R^1$  and  $R^2$  independently are hydrogen, halo, hydroxy,  $C_1$ - $C_6$  alkyl,

$C_1$ - $C_6$  alkoxy,  $C_2$ - $C_6$  alkenyl,  $C_2$ - $C_6$  alkynyl,  $NO_2$ ,  $NR^4R^5$ , CN, or  $CF_3$ ;

$R^4$  and  $R^5$  independently are H,  $C_1$ - $C_6$  alkyl,  $C_2$ - $C_6$  alkenyl,  $C_2$ - $C_6$

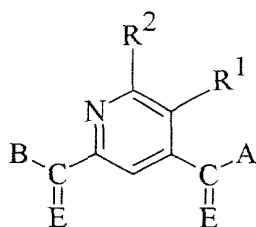
alkynyl,  $(CH_2)_n$  aryl,  $(CH_2)_n$  cycloalkyl,  $(CH_2)_n$  heteroaryl, or  $R^4$

and  $R^5$  when taken together with the nitrogen to which they are attached complete a 3- to 8-membered ring containing carbon atoms and optionally containing a heteroatom selected from O, S, or NH, and optionally substituted or unsubstituted;

Each Ar is independently aryl or Het, wherein aryl is phenyl or substituted phenyl;

Het is an unsubstituted or substituted heteroaryl group.

6. A compound of Formula I



I

or a pharmaceutically acceptable salt thereof,  
wherein

$R^1$  and  $R^2$  independently are hydrogen, halo, hydroxy,  $C_1$ - $C_6$  alkyl,

5  $C_1$ - $C_6$  alkoxy,  $C_2$ - $C_6$  alkenyl,  $C_2$ - $C_6$  alkynyl,  $NO_2$ ,  $NR^4R^5$ , CN,  
or  $CF_3$ ;

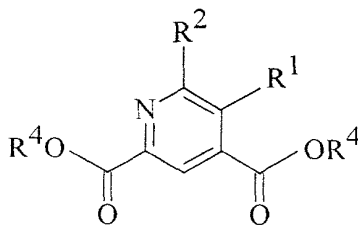
E is independently O or S;

A and B independently are  $OR^4$  or  $NR^4R^5$ ;

$R^4$  and  $R^5$  independently are H,  $C_1$ - $C_6$  alkyl,  $C_2$ - $C_6$  alkenyl,  $C_2$ - $C_6$   
10 alkynyl,  $(CH_2)_n$  aryl,  $(CH_2)_n$  cycloalkyl,  $(CH_2)_n$  heteroaryl, or  $R^4$   
and  $R^5$  when taken together with the nitrogen to which they are  
attached complete a 3- to 8-membered ring containing carbon  
atoms and optionally containing a heteroatom selected from O, S,  
or NH, and optionally substituted or unsubstituted;

15 n is an integer from 0 to 6.

7. A compound of Formula II



II

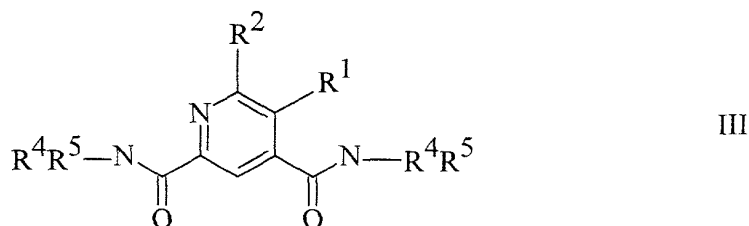
or a pharmaceutically acceptable salt thereof,

20 wherein  $R^1$  and  $R^2$  independently are hydrogen, halo, hydroxy,  $C_1$ - $C_6$   
alkyl,  $C_1$ - $C_6$  alkoxy,  $C_2$ - $C_6$  alkenyl,  $C_2$ - $C_6$  alkynyl,  $NO_2$ ,  
 $NR^4R^5$ , CN, or  $CF_3$ ; and

each  $R^4$  and  $R^5$  independently are H,  $C_1$ - $C_6$  alkyl,  $C_2$ - $C_6$  alkenyl,  $C_2$ - $C_6$  alkynyl,  $(CH_2)_n$  aryl,  $(CH_2)_n$  cycloalkyl,  $(CH_2)_n$  heteroaryl, or  $R^4$  and  $R^5$  when taken together with the nitrogen to which they are attached complete a 3- to 8-membered ring containing carbon atoms and optionally containing a heteroatom selected from O, S, or NH, and optionally substituted or unsubstituted;

$n$  is an integer of from 0 to 6.

8. A compound of Formula III



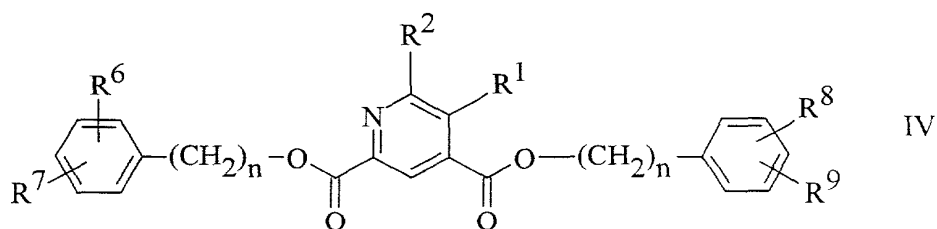
or a pharmaceutically acceptable salt thereof,

wherein  $R^1$  and  $R^2$  independently are hydrogen, halo, hydroxy,  $C_1$ - $C_6$  alkyl,  $C_1$ - $C_6$  alkoxy,  $C_2$ - $C_6$  alkenyl,  $C_2$ - $C_6$  alkynyl,  $NO_2$ ,  $NR^4R^5$ , CN, or  $CF_3$ ;

Each  $R^4$  and  $R^5$  independently are H,  $C_1$ - $C_6$  alkyl,  $C_2$ - $C_6$  alkenyl,  $C_2$ - $C_6$  alkynyl,  $(CH_2)_n$  aryl,  $(CH_2)_n$  cycloalkyl,  $(CH_2)_n$  heteroaryl, wherein each  $CH_2$  is optionally substituted by one or more  $C_1$ - $C_6$  alkyl, or  $R^4$  and  $R^5$  when taken together with the nitrogen to which they are attached complete a 3- to 8-membered ring containing carbon atoms and optionally containing a heteroatom selected from O, S, or NH, and optionally substituted or unsubstituted;

$n$  is an integer of from 0 to 6.

9. A compound of Formula IV



or a pharmaceutically acceptable salt thereof,

wherein n is 0 to 6;

R<sup>1</sup> and R<sup>2</sup> independently are hydrogen, halo, hydroxy, C<sub>1</sub>-C<sub>6</sub> alkyl,

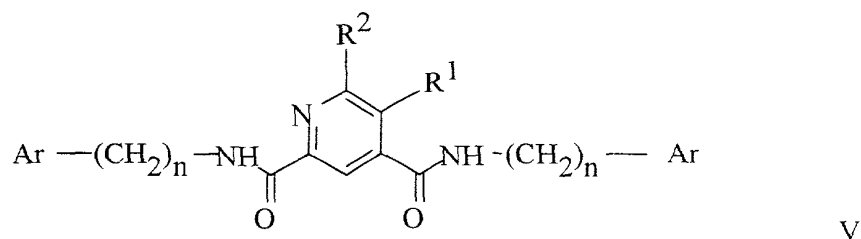
5 C<sub>1</sub>-C<sub>6</sub> alkoxy, C<sub>2</sub>-C<sub>6</sub> alkenyl, C<sub>2</sub>-C<sub>6</sub> alkynyl, NO<sub>2</sub>, NR<sup>4</sup>R<sup>5</sup>, CN,  
or CF<sub>3</sub>;

R<sup>4</sup> and R<sup>5</sup> independently are H, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>2</sub>-C<sub>6</sub> alkenyl, C<sub>2</sub>-C<sub>6</sub>  
alkynyl, (CH<sub>2</sub>)<sub>n</sub> aryl, (CH<sub>2</sub>)<sub>n</sub> cycloalkyl, (CH<sub>2</sub>)<sub>n</sub> heteroaryl,

10 wherein each CH<sub>2</sub> is optionally substituted by one or more C<sub>1</sub>-C<sub>6</sub>  
alkyl, or R<sup>4</sup> and R<sup>5</sup> when taken together with the nitrogen to which  
they are attached complete a 3- to 8-membered ring containing  
carbon atoms and optionally containing a heteroatom selected from  
O, S, or NH, and optionally substituted or unsubstituted; and

15 R<sup>6</sup>, R<sup>7</sup>, R<sup>8</sup>, and R<sup>9</sup> independently are hydrogen, halo, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-C<sub>6</sub>  
alkoxy, nitro, or NH<sub>2</sub>

10 A compound of Formula V



or a pharmaceutically acceptable salt thereof,

wherein n is 0 to 6;

R<sup>1</sup> and R<sup>2</sup> independently are hydrogen, halo, hydroxy, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-C<sub>6</sub> alkoxy, C<sub>2</sub>-C<sub>6</sub> alkenyl, C<sub>2</sub>-C<sub>6</sub> alkynyl, NO<sub>2</sub>, NR<sup>4</sup>R<sup>5</sup>, CN, or CF<sub>3</sub>;

R<sup>4</sup> and R<sup>5</sup> independently are H, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>2</sub>-C<sub>6</sub> alkenyl, C<sub>2</sub>-C<sub>6</sub> alkynyl, (CH<sub>2</sub>)<sub>n</sub> aryl, (CH<sub>2</sub>)<sub>n</sub> cycloalkyl, (CH<sub>2</sub>)<sub>n</sub> heteroaryl, or R<sup>4</sup> and R<sup>5</sup> when taken together with the nitrogen to which they are attached complete a 3- to 8-membered ring containing carbon atoms and optionally containing a heteroatom selected from O, S, or NH, and optionally substituted or unsubstituted;

Each Ar is independently aryl or Het, wherein aryl is phenyl or substituted phenyl;

Het is an unsubstituted or substituted heteroaryl group.

11. A compound selected from:

Pyridine-2,4-dicarboxylic acid bis-(3-methoxy-benzylamide);

Pyridine-3,5-dicarboxylic acid bis-(4-chloro-benzylamide);

Pyridine-3,5-dicarboxylic acid bis-(3-chloro-benzylamide);

2-Methoxy-pyridine-3,5-dicarboxylic acid bis-[(1,3-benzodioxol-5-ylmethyl)-amide];

Pyridine-3,5-dicarboxylic acid bis-(1,3-benzodioxol-5-ylmethyl)

ester;

Pyridine-3,5-dicarboxylic acid bis-(4-methoxy-benzylamide);

Pyridine-3,5-dicarboxylic acid bis-[(1,3-benzodioxol-5-ylmethyl)-amide],

Pyridine-2,4-dicarboxylic acid bis-[(1,3-benzodioxol-5-ylmethyl)-amide],

Pyridine-3,5-dicarboxylic acid bis-(4-fluoro-benzylamide);

Pyridine-3,5-dicarboxylic acid, (4-chloro-benzylamide), [(1,3-benzodioxol-5-ylmethyl)-amide];

Pyridine-3,5-dicarboxylic acid, (4-carboxy-benzylamide), [(1,3-benzodioxol-5-ylmethyl)-amide],



Pyridine-3,5-dicarboxylic acid, (4-carboxy-benzylamide), (4-methoxy-benzylamide),

Pyridine-3,5-dicarboxylic acid, (4-carboxy-benzylamide), (3-methoxy-benzylamide);

5 Pyridine-3,5-dicarboxylic acid, (4-carbomethoxy-benzylamide), (3-methoxy-benzylamide);

Pyridine-3,5-dicarboxylic acid, (4-carboxy-benzylamide), (3-pyridylmethylamide);

10 Pyridine-3,5-dicarboxylic acid, (4-carboxy-benzylamide), (3-thiophenemethylamide);

Pyridine-3,5-dicarboxylic acid, (2,1,3-benzothiadiazol-5-ylmethyl) amide, [(1,3-benzodioxol-5-ylmethyl)-amide];

Pyridine-3,5-dicarboxylic acid, (2,1,3-benzooxadiazol-5-ylmethyl) amide, [(1,3-benzodioxol-5-ylmethyl)-amide],

15 Pyridine-3,5-dicarboxylic acid, (2,1,3-benzothiadiazol-5-ylmethyl) amide, (4-methoxy-benzylamide),

Pyridine-3,5-dicarboxylic acid, (2,1,3-benzothiadiazol-5-ylmethyl) amide, (3-methoxy-benzylamide);

20 Pyridine-3,5-dicarboxylic acid bis-(1,3-benzodioxol-5-ylmethyl) ester;

2-Methoxy-pyridine-3,5-dicarboxylic acid bis-[(1,3-benzodioxol-5-ylmethyl)-amide];

2-Ethoxy-pyridine-3,5-dicarboxylic acid bis-[(1,3-benzodioxol-5-ylmethyl)-amide];

25 2-Oxo-1,2-dihydro-pyridine-3,5-dicarboxylic acid bis-benzylamide;

2-Methoxy-pyridine-3,5-dicarboxylic acid bis-benzylamide,

(3,5-Bis-benzylcarbamoyl-pyridin-2-yloxy)-acetic acid tert-butyl ester,

30 (3,5-Bis-benzylcarbamoyl-pyridin-2-yloxy)-acetic acid,

Pyridine-2,4-dicarboxylic acid bis-(3-methoxy-benzylamide),

Pyridine-2,4-dicarboxylic acid bis-[(1,3-benzodioxol-5-ylmethyl)-amide];

Pyridine-2,4-dicarboxylic acid bis-(2,4-dimethoxy-benzylamide),

Pyridine-2,4-dicarboxylic acid bis-(4-chloro-benzylamide);

Pyridine-2,4-dicarboxylic acid bis-benzylamide;

Pyridine-2,4-dicarboxylic acid bis-[(naphthalen-1-ylmethyl)-  
amide],

Pyridine-2,4-dicarboxylic acid bis-[(2-p-tolyl-ethyl)-amide];

Pyridine-2,4-dicarboxylic acid bis-(4-methoxy-benzylamide);

Pyridine-2,4-dicarboxylic acid bis-(3-fluoro-benzylamide),

Pyridine-2,4-dicarboxylic acid bis-(benzyl-ethyl-amide);

Pyridine-2,4-dicarboxylic acid bis-{[2-(3,4-dimethoxy-phenyl)-  
ethyl]-amide};

Pyridine-2,4-dicarboxylic acid bis-{[2-(2-phenoxy-phenyl)-ethyl]-  
amide};

Pyridine-2,4-dicarboxylic acid bis-[(4-phenyl-butyl)-amide];

Pyridine-2,4-dicarboxylic acid bis-{[2-(4-methoxy-phenyl)-ethyl]-  
amide};

Pyridine-2,4-dicarboxylic acid bis-{[2-(2-fluoro-phenyl)-ethyl]-  
amide},

Pyridine-2,4-dicarboxylic acid bis-{[2-(3-chloro-phenyl)-ethyl]-  
amide},

Pyridine-2,4-dicarboxylic acid bis-{[2-(2,4-dimethyl-phenyl)-  
ethyl]-amide};

Pyridine-2,4-dicarboxylic acid bis-[(2-o-tolyl-ethyl)-amide];

Pyridine-2,4-dicarboxylic acid bis-{[2-(4-ethyl-phenyl)-ethyl]-  
amide};

Pyridine-2,4-dicarboxylic acid bis-[(2-phenyl-propyl)-amide];

Pyridine-2,4-dicarboxylic acid bis-[(1,2-diphenyl-ethyl)-amide];

Pyridine-2,4-dicarboxylic acid bis-(2,4-dichloro-benzylamide);

Pyridine-2,4-dicarboxylic acid bis-[(biphenyl-2-ylmethyl)-amide];

Pyridine-2,4-dicarboxylic acid bis-(3,4,5-trimethoxy-benzylamide);

Pyridine-2,4-dicarboxylic acid bis-(3-chloro-benzylamide);

Pyridine-2,4-dicarboxylic acid bis-(3,5-dimethoxy-benzylamide),

Pyridine-2,4-dicarboxylic acid bis-(3,4-dimethoxy-benzylamide),

Pyridine-2,4-dicarboxylic acid bis-(ethyl-pyridin-4-ylmethyl-  
amide);

Pyridine-2,4-dicarboxylic acid bis-[(2-pyridin-4-yl-ethyl)-amide];

Pyridine-2,4-dicarboxylic acid bis-[(2-pyridin-3-yl-ethyl)-amide];

5 Pyridine-2,4-dicarboxylic acid bis-{[2-(4-chloro-phenyl)-ethyl]-  
amide};

Pyridine-2,4-dicarboxylic acid bis-[(pyridin-4-ylmethyl)-amide];

Pyridine-2,4-dicarboxylic acid bis-(3,5-bis-trifluoromethyl-  
benzylamide),

10 Pyridine-2,4-dicarboxylic acid bis-(2,3-dimethoxy-benzylamide);

Pyridine-2,4-dicarboxylic acid bis-(3-trifluoromethyl-  
benzylamide);

Pyridine-2,4-dicarboxylic acid bis-(2-trifluoromethoxy-  
benzylamide);

15 Pyridine-2,4-dicarboxylic acid bis-(3-difluoromethoxy-  
benzylamide);

Pyridine-2,4-dicarboxylic acid bis-(2-difluoromethoxy-  
benzylamide);

20 Pyridine-2,4-dicarboxylic acid bis-(4-fluoro-3-trifluoromethyl-  
benzylamide);

Pyridine-2,4-dicarboxylic acid bis-(2-methoxy-benzylamide);

Pyridine-2,4-dicarboxylic acid bis-{[2-(3-ethoxy-phenyl)-ethyl]-  
amide};

25 Pyridine-2,4-dicarboxylic acid bis-(3-chloro-4-fluoro-  
benzylamide);

Pyridine-2,4-dicarboxylic acid bis-(2,4-difluoro-benzylamide),

Pyridine-2,4-dicarboxylic acid bis-(4-amino-benzylamide),

Pyridine-2,4-dicarboxylic acid bis-(2-methyl-benzylamide);

30 Pyridine-2,4-dicarboxylic acid bis-{[bis-(4-methoxy-phenyl)-  
methyl]-amide};

Pyridine-2,4-dicarboxylic acid bis-[(3,3-diphenyl-propyl)-amide];

Pyridine-2,4-dicarboxylic acid bis-[(1-methyl-3-phenyl-propyl)-  
amide];

Pyridine-2,4-dicarboxylic acid bis-[(3,4-dimethoxy-phenyl)-amide];

Pyridine-2,4-dicarboxylic acid bis-(2-fluoro-benzylamide);

Pyridine-2,4-dicarboxylic acid bis-[(3-imidazol-1-yl-propyl)-amide];

Pyridine-2,4-dicarboxylic acid bis-(2-chloro-benzylamide);

Pyridine-2,4-dicarboxylic acid bis-(2-trifluoromethyl-benzylamide);

Pyridine-2,4-dicarboxylic acid bis-(4-methyl-benzylamide);

Pyridine-2,4-dicarboxylic acid bis-{[2-(3-methoxy-phenyl)-ethyl]-amide}.

Pyridine-2,4-dicarboxylic acid bis-[(1-phenyl-ethyl)-amide],

Pyridine-2,4-dicarboxylic acid bis-[(pyridin-3-ylmethyl)-amide];

Pyridine-2,4-dicarboxylic acid bis-[(4-ethoxy-phenyl)-amide];

Pyridine-2,4-dicarboxylic acid bis-(phenethyl-amide);

Pyridine-2,4-dicarboxylic acid bis-[(thiophen-2-ylmethyl)-amide];

Pyridine-2,4-dicarboxylic acid bis-(4-trifluoromethyl-benzylamide);

Pyridine-2,4-dicarboxylic acid bis-[(5-methyl-furan-2-ylmethyl)-amide];

Pyridine-2,4-dicarboxylic acid bis-{[1-(4-fluoro-phenyl)-ethyl]-amide},

Pyridine-2,4-dicarboxylic acid bis-(2-amino-benzylamide);

Pyridine-2,4-dicarboxylic acid bis-[(1-naphthalen-1-yl-ethyl)-amide],

Pyridine-2,4-dicarboxylic acid bis-{[2-(4-hydroxy-phenyl)-ethyl]-amide};

Pyridine-2,4-dicarboxylic acid bis-(3-trifluoromethoxy-benzylamide);

Pyridine-2,4-dicarboxylic acid bis-{[1-(3-methoxy-phenyl)-ethyl]-amide};

Pyridine-2,4-dicarboxylic acid bis-[(1-phenyl-propyl)-amide];

Pyridine-2,4-dicarboxylic acid bis- {[2-(2-methoxy-phenyl)-ethyl]-amide};

Pyridine-2,4-dicarboxylic acid bis- {[2-(3-trifluoromethyl-phenyl)-ethyl]-amide};

5 Pyridine-2,4-dicarboxylic acid bis-indan-1-ylamide,

Pyridine-2,4-dicarboxylic acid bis-indan-1-ylamide;

Pyridine-2,4-dicarboxylic acid bis-(3,4-dichloro-benzylamide);

Pyridine-2,4-dicarboxylic acid bis-[(2-ethoxy-ethyl)-amide];

10 Pyridine-2,4-dicarboxylic acid bis- {[2-(4-bromo-phenyl)-ethyl]-amide};

Pyridine-2,4-dicarboxylic acid bis-[(2-pyridin-2-yl-ethyl)-amide];

Pyridine-2,4-dicarboxylic acid bis-[(2-thiophen-2-yl-ethyl)-amide];

Pyridine-2,4-dicarboxylic acid bis- {[2-(5-methoxy-1H-indol-3-yl)-ethyl]-amide};

15 Pyridine-2,4-dicarboxylic acid bis- {[2-(1H-indol-3-yl)-ethyl]-amide},

Pyridine-2,4-dicarboxylic acid bis-(3,5-dichloro-benzylamide); and

2-Amino-pyridine-3,5-dicarboxylic acid bis-[(1,3-benzodioxol-5-ylmethyl)-amide]

20 12. A pharmaceutical composition, comprising a compound of Claim 6, or a pharmaceutically acceptable salt thereof, together with a pharmaceutically acceptable carrier, diluent, or excipient.

25 13. A pharmaceutical composition, comprising a compound of Claim 7, or a pharmaceutically acceptable salt thereof, together with a pharmaceutically acceptable carrier, diluent, or excipient.

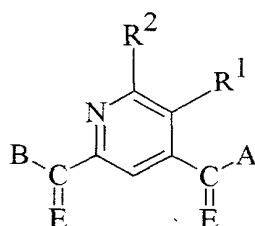
30 14. A pharmaceutical composition, comprising a compound of Claim 8, or a pharmaceutically acceptable salt thereof, together with a pharmaceutically acceptable carrier, diluent, or excipient.

15. A pharmaceutical composition, comprising a compound of Claim 9, or a pharmaceutically acceptable salt thereof, together with a pharmaceutically acceptable carrier, diluent, or excipient.
- 5 16. A pharmaceutical composition, comprising a compound of Claim 10, or a pharmaceutically acceptable salt thereof, together with a pharmaceutically acceptable carrier, diluent, or excipient.
- 10 17. A pharmaceutical composition, comprising a compound of Claim 11, or a pharmaceutically acceptable salt thereof, together with a pharmaceutically acceptable carrier, diluent, or excipient.
18. A method for inhibiting an MMP-13 enzyme in an animal, comprising administering to the animal an MMP-13 inhibiting amount of a compound of Claim 6, or a pharmaceutically acceptable salt thereof.
- 15 19. A method for treating a cancer, comprising administering to a patient having cancer and in need of treatment an anticancer effective amount of a compound of Claim 6, or a pharmaceutically acceptable salt thereof
- 20 20. A method for treating breast carcinoma, comprising administering to a patient having cancer and in need of treatment an anticancer effective amount of a compound of Claim 6, or a pharmaceutically acceptable salt thereof
21. A method for treating osteoarthritis, comprising administering to a patient in need of treatment an effective amount of a compound of Claim 6, or a pharmaceutically acceptable salt thereof
- 25 22. A method for treating rheumatoid arthritis, comprising administering to a patient in need of treatment an effective amount of a compound of Claim 6, or a pharmaceutically acceptable salt thereof

23. A method for treating inflammation, comprising administering to a patient in need of treatment an effective amount of a compound of Claim 6, or a pharmaceutically acceptable salt thereof.

5 24. A method for treating heart failure, comprising administering to a patient in need of treatment an effective amount of a compound of Claim 6, or a pharmaceutically acceptable salt thereof.

10 25. A method for inhibiting matrix metalloproteinase enzymes in a mammal comprising administering an MMP inhibiting amount of a compound of Formula I



I

wherein:

$R^1$  and  $R^2$  independently are hydrogen, halo, hydroxy,  $C_1$ - $C_6$  alkyl,

$C_1$ - $C_6$  alkoxy,  $C_2$ - $C_6$  alkenyl,  $C_2$ - $C_6$  alkynyl,  $NO_2$ ,  $NR^4R^5$ , CN,

or  $CF_3$ ;

E is independently O or S;

A and B independently are  $OR^4$  or  $NR^4R^5$ ,

$R^4$  and  $R^5$  independently are H,  $C_1$ - $C_6$  alkyl,  $C_2$ - $C_6$  alkenyl,  $C_2$ - $C_6$

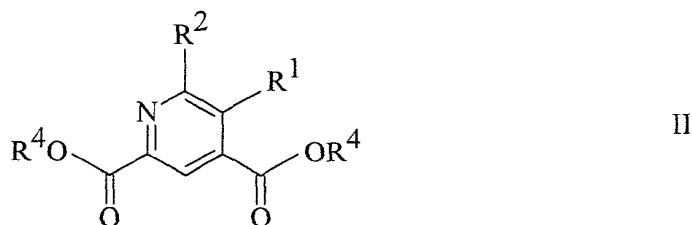
alkynyl,  $(CH_2)_n$  aryl,  $(CH_2)_n$  cycloalkyl,  $(CH_2)_n$  heteroaryl, or  $R^4$

and  $R^5$  when taken together with the nitrogen to which they are attached complete a 3- to 8-membered ring, optionally containing a heteroatom selected from O, S, or NH, and optionally substituted or unsubstituted;

n is an integer from 0 to 6;

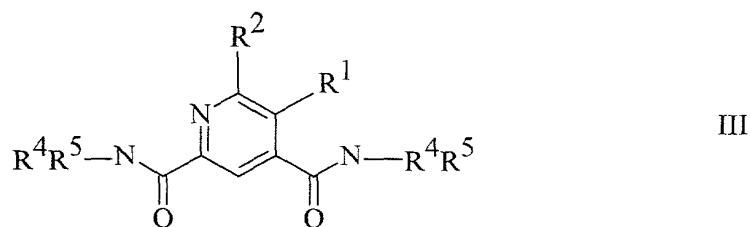
and the pharmaceutically acceptable salts thereof.

- 26 A method for inhibiting matrix metalloproteinase enzymes in a mammal comprising administering an MMP inhibiting amount of a compound of Formula II



- 5 wherein R<sup>1</sup> and R<sup>2</sup> independently are hydrogen, halo, hydroxy, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-C<sub>6</sub> alkoxy, C<sub>2</sub>-C<sub>6</sub> alkenyl, C<sub>2</sub>-C<sub>6</sub> alkynyl, NO<sub>2</sub>, NR<sup>4</sup>R<sup>5</sup>, CN, or CF<sub>3</sub>; and  
 each R<sup>4</sup> is independently H, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>2</sub>-C<sub>6</sub> alkenyl, C<sub>2</sub>-C<sub>6</sub> alkynyl, (CH<sub>2</sub>)<sub>n</sub> aryl, (CH<sub>2</sub>)<sub>n</sub> cycloalkyl, (CH<sub>2</sub>)<sub>n</sub> heteroaryl,  
 10 and the pharmaceutically acceptable salts thereof

27. A method for inhibiting matrix metalloproteinase enzymes in a mammal comprising administering an MMP inhibiting amount of a compound of Formula III

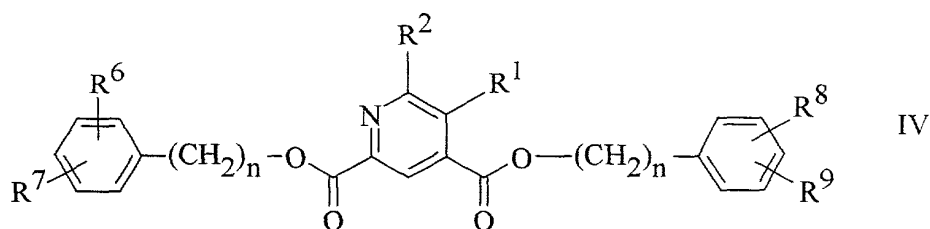


- 15 wherein R<sup>1</sup> and R<sup>2</sup> independently are hydrogen, halo, hydroxy, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-C<sub>6</sub> alkoxy, C<sub>2</sub>-C<sub>6</sub> alkenyl, C<sub>2</sub>-C<sub>6</sub> alkynyl, NO<sub>2</sub>, NR<sup>4</sup>R<sup>5</sup>, CN, or CF<sub>3</sub>,  
 R<sup>4</sup> and R<sup>5</sup> independently are H, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>2</sub>-C<sub>6</sub> alkenyl, C<sub>2</sub>-C<sub>6</sub> alkynyl, (CH<sub>2</sub>)<sub>n</sub> aryl, (CH<sub>2</sub>)<sub>n</sub> cycloalkyl, (CH<sub>2</sub>)<sub>n</sub> heteroaryl, or R<sup>4</sup>  
 20 and R<sup>5</sup> when taken together with the nitrogen to which they are attached complete a 3- to 8-membered ring, optionally containing a



heteroatom selected from O, S, or NH, and optionally substituted or unsubstituted;  
and the pharmaceutically acceptable salts thereof.

- 28 A method for inhibiting matrix metalloproteinase enzymes in a mammal  
5 comprising administering an MMP inhibiting amount of a compound of  
Formula IV



wherein n is 0 to 6;

R<sup>1</sup> and R<sup>2</sup> independently are hydrogen, halo, hydroxy, C<sub>1</sub>-C<sub>6</sub> alkyl,

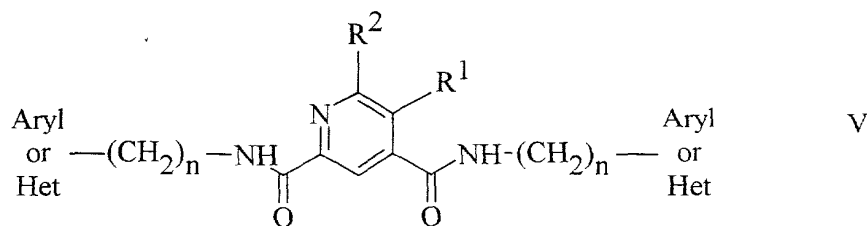
10 C<sub>1</sub>-C<sub>6</sub> alkoxy, C<sub>2</sub>-C<sub>6</sub> alkenyl, C<sub>2</sub>-C<sub>6</sub> alkynyl, NO<sub>2</sub>, NR<sup>4</sup>R<sup>5</sup>, CN,

or CF<sub>3</sub>; and R<sup>6</sup>, R<sup>7</sup>, R<sup>8</sup>, and R<sup>9</sup> independently are hydrogen, halo,

C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-C<sub>6</sub> alkoxy, nitro, or NH<sub>2</sub>;

and the pharmaceutically acceptable salts thereof.

29. A method for inhibiting matrix metalloproteinase enzymes in a mammal  
15 comprising administering an MMP inhibiting amount of a compound of  
Formula V



wherein n is 0 to 6,

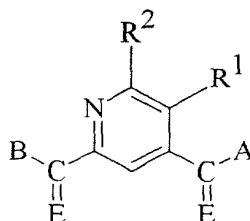
R<sup>1</sup> and R<sup>2</sup> independently are hydrogen, halo, hydroxy, C<sub>1</sub>-C<sub>6</sub> alkyl,

20 C<sub>1</sub>-C<sub>6</sub> alkoxy, C<sub>2</sub>-C<sub>6</sub> alkenyl, C<sub>2</sub>-C<sub>6</sub> alkynyl, NO<sub>2</sub>, NR<sup>4</sup>R<sup>5</sup>, CN,

or CF<sub>3</sub>;

Aryl is phenyl or substituted phenyl;  
 Het is an unsubstituted or substituted heteroaryl group;  
 and the pharmaceutically acceptable salts thereof.

30. A compound having Formula I



$R^1$  and  $R^2$  independently are hydrogen, halo, hydroxy,  $C_1$ - $C_6$  alkyl,  $C_1$ - $C_6$  alkoxy,  $C_2$ - $C_6$  alkenyl,  $C_2$ - $C_6$  alkynyl,  $NO_2$ ,  $NR^4R^5$ , CN, or  $CF_3$ ;

E is independently O or S;

A and B independently are  $OR^4$  or  $NR^4R^5$ ;

$R^4$  and  $R^5$  independently are H,  $C_1$ - $C_6$  alkyl,  $C_2$ - $C_6$  alkenyl,  $C_2$ - $C_6$  alkynyl,  $(CH_2)_n$  aryl,  $(CH_2)_n$  cycloalkyl,  $(CH_2)_n$  heteroaryl, or  $R^4$  and  $R^5$  when taken together with the nitrogen to which they are attached complete a 3- to 8-membered ring, optionally containing a heteroatom selected from O, S, or NH, and optionally substituted or unsubstituted;

n is an integer from 0 to 6,

and the pharmaceutically acceptable salts thereof.

31. A compound selected from

Pyridine-2,4-dicarboxylic acid bis-(3-methoxy-benzylamide),  
 Pyridine-3,5-dicarboxylic acid bis-(4-chloro-benzylamide),  
 Pyridine-3,5-dicarboxylic acid bis-(3-chloro-benzylamide);  
 2-Methoxy-pyridine-3,5-dicarboxylic acid bis-[(1,3-benzodioxol-5-ylmethyl)-amide];

Pyridine-3,5-dicarboxylic acid bis-(1,3-benzodioxol-5-ylmethyl)  
ester;

Pyridine-3,5-dicarboxylic acid bis-(4-methoxy-benzylamide);

Pyridine-3,5-dicarboxylic acid bis-[(1,3-benzodioxol-5-ylmethyl)-  
amide];

Pyridine-2,4-dicarboxylic acid bis-[(1,3-benzodioxol-5-ylmethyl)-  
amide];

Pyridine-3,5-dicarboxylic acid bis-(4-fluoro-benzylamide);

Pyridine-3,5-dicarboxylic acid, (4-chloro-benzylamide), [(1,3-  
benzodioxol-5-ylmethyl)-amide];

Pyridine-3,5-dicarboxylic acid, (4-carboxy-benzylamide), [(1,3-  
benzodioxol-5-ylmethyl)-amide];

Pyridine-3,5-dicarboxylic acid, (4-carboxy-benzylamide), (4-  
methoxy-benzylamide);

Pyridine-3,5-dicarboxylic acid, (4-carboxy-benzylamide), (3-  
methoxy-benzylamide);

Pyridine-3,5-dicarboxylic acid, (4-carbomethoxy-benzylamide), (3-  
methoxy-benzylamide);

Pyridine-3,5-dicarboxylic acid, (4-carboxy-benzylamide), (3-  
pyridylmethylamide);

Pyridine-3,5-dicarboxylic acid, (4-carboxy-benzylamide), (3-  
thiophenemethylamide);

Pyridine-3,5-dicarboxylic acid, (2,1,3-benzothiadiazol-5-ylmethyl)  
amide, [(1,3-benzodioxol-5-ylmethyl)-amide];

Pyridine-3,5-dicarboxylic acid, (2,1,3-benzooxadiazol-5-ylmethyl)  
amide, [(1,3-benzodioxol-5-ylmethyl)-amide];

Pyridine-3,5-dicarboxylic acid, (2,1,3-benzothiadiazol-5-ylmethyl)  
amide, (4-methoxy-benzylamide);

Pyridine-3,5-dicarboxylic acid, (2,1,3-benzothiadiazol-5-ylmethyl)  
amide, (3-methoxy-benzylamide);

Pyridine-3,5-dicarboxylic acid bis-(1,3-benzodioxol-5-ylmethyl)  
ester;

2-Methoxy-pyridine-3,5-dicarboxylic acid bis-[(1,3-benzodioxol-5-ylmethyl)-amide],

2-Ethoxy-pyridine-3,5-dicarboxylic acid bis-[(1,3-benzodioxol-5-ylmethyl)-amide]; and

5           2-Amino-pyridine-3,5-dicarboxylic acid bis-[(1,3-benzodioxol-5-ylmethyl)-amide].

32.    A pharmaceutical composition comprising a compound of Claim 30 together with a pharmaceutically acceptable carrier, diluent, or excipient

10    33.    A method for inhibiting MMP-13 enzymes in animals comprising administering to the animal an MMP-13 inhibiting amount of a compound of Claim 30.

34.    A method for treating cancer comprising administering to a patient having cancer and in need of treatment an anticancer effective amount of a compound of Claim 30

15    35    A method for treating osteoarthritis or rheumatoid arthritis comprising administering to a patient in need of treatment an effective amount of a compound of Claim 30.